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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,503	06/07/2001	Hiroshi Oda	11283-009001	1563

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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,503	ODA ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21 and 37-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21 and 37-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The Request for Continued Examination and amendment filed November 12, 2004 is acknowledged and has been entered.

Election/Restrictions

Applicant's amendments to claims 37-40 are acknowledged and after consideration of the amendments the restriction requirement of claims 37-40 is withdrawn. Thus claims 21 and 37-43 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 21 and 37-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a comparison step comparing the concentration of human L-PGDS in the test subject to the concentration of L-PGDS of normal healthy subjects. It is recommended to insert a comparison step after the step of determining a concentration of human lipocalin-type prostaglandin D synthase and before the recitation "wherein a higher concentration of human L-PGDS". See also deficiencies found in claims 37-40.

Claim 21 is vague and indefinite because the claim does not define what a reference value of human L-PGDS is. For example, if the reference value is a low L-PGDS control does the comparison to a test subject with an increased L-PGDS as compared to the low level control indicate early-stage renal disease. On page 9, lines 19-25 in the specification, Applicant discloses that a reference value set by determining the concentrations of L-PGDS in body fluid samples taken from healthy subjects. It appears that the reference value must come from healthy subjects in order to properly work. See also deficiencies found in claims 37-40.

Claim 37, lines 3-4 the recitation "the concentration of creatinine in the serum of the test subject being normal" is vague and indefinite. It is unclear if this is part of the method or not. It is unclear if this is another step of the currently recited method in which creatinine concentration of the test subject is also determined or if the concentration of the creatinine is determined in another method outside of the recited method.

Claim 38, lines 3-4 the recitation "the test subject not exhibiting proteinuria" there is insufficient antecedent basis for this limitation.

Claim 38, lines 3-4 the recitation "the test subject not exhibiting proteinuria". It is unclear if it is part of the method or not. It is unclear if this is another step of the currently recited method in which protein concentration of the test subject's urine is also determined or if the concentration of the protein in urine of the test subject is determined in another method outside of the recited method.

Claim 39 , lines 3-4 the recitation "the concentration of albumin in the urine of the test subject being normal". It is unclear if it is part of the method or not. It is unclear if this is another step of the currently recited method in which urine albumin concentration of the test subject is also determined or if the concentration of the urine albumin is determined in another method outside of the recited method.

Claim 40 the recitation "the test subject not exhibiting proteinuria" there is insufficient antecedent basis for this limitation.

Claim 40, lines 3-5 the recitation "the concentration of creatinine in the serum of the test subject being normal, the concentration of albumin in the urine of the test subject being normal, and the test subject not exhibiting proteinuria. It is unclear if these are part of the method or not. It is unclear if these are methods steps of the currently recited method or if they are determined in another method outside of the recited method.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 21, and 37-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoffman et al (Molecular characterization of beta-trace protein in human serum and urine: a potential diagnostic marker for renal disease, Gylcobiology, vol 7, no 4 p 499-506 (1997)).

Hoffman et al disclose that beta-trace protein (lipocalin-type prostaglandin D synthase (L-PGDS)) was isolated from cerebrospinal fluid, serum, plasma and urine samples of normal volunteers and sera and hemofiltrate of patients with chronic renal failure (abstract). Hoffman et al disclose that serum L-PGDS concentration in patients with end-stage renal failure increased as compared to the L-PGDS of the normal volunteers. Hoffman et al disclose that serum beta-trace (L-PGDS) concentrations were determined by quantitative immunoaffinity chromatography in conjunction with amino

acid sequencing and SDS gel electrophoresis and revealed a broad range of concentrations (p. 504, col 2, lines 36-60).

Even tough Hoffman et al is silent on a method of detection of an early-stage renal disease, Hoffman et al teaches that beta-trace protein (L-PGDS) accumulates more significantly in serum in pathological conditions than other proteins in current use and that the beta-trace protein may be used for the study and early diagnosis of renal diseases (p. 505, lines 14-21). Therefore, it would have been obvious to one of ordinary skill in the art to have a reasonable expectation of success to use the method of Hoffman et al for the detection of early-stage renal disease.

With respect to a urine sample as recited in the instant claims. Hoffman et al disclose that the proteins of urinary and serum-derived beta-trace proteins are identical (p. 501 and 504) and Hoffman et al further teaches the detection of beta-trace proteins in urine. Hoffman et al specifically teaches that in renal diseases that the elimination of proteins through the kidney is disturbed resulting in elevated concentrations of proteins and Hoffman et al also teaches higher levels of L-PGDS in renal failure patients. Therefore, it would have been obvious to one of ordinary skill in the art to use urine as the sample for beta-trace proteins. Further, Hoffman et al also teaches that proteins are elevated in renal disease, and that L-PDGS may be used for the study and early diagnosis of renal diseases, Therefore, one of ordinary skill in the art would expect increased levels of L-PGDS in the urine of renal disease patients and one of ordinary skill in the art would have a reasonable expectation of success to use urine as a

sample and use the method of Hoffman et al for the detection of early-stage renal disease.

Response to Arguments

7. Applicant's arguments filed November 12, 2004 have been fully considered but they are not persuasive.

Applicant argues that finding made in serum cannot without appropriate experimentation be extrapolated to other bodily fluids such as urine. Applicant refers to Hirawa et al, Nephron 87: 321-327 and point out that the Hirawa et al reference emphasizes that blood and urine levels of a substance are not always proportionately correlated. This is not found persuasive because Applicant is relying on the teaching that plasma concentrations are independent of urine concentrations. Examiner has not relied upon Hoffman for teaching the two are independent of one another, but Examiner has rather relied upon Hoffman et al teach that L-PGDS can be found in both serum and urine sample and that the proteins are identical. Hoffman specifically teaches that in renal diseases that the elimination of proteins through the kidney is disturbed resulting in elevated concentrations of proteins and since Hoffman et al teaches higher levels of L-PGDS in renal failure patients and specifically teaches that this protein is identical in serum and urine, it would have been obvious to one of ordinary skill in the art to use a urine sample as the sample for beta-trace proteins. Hoffman et al also teaches that proteins are elevated in renal disease, and that L-PDGS may be used for the study and early diagnosis of renal diseases. Therefore, one of ordinary skill in the art would expect increased levels of L-PGDS in the urine of renal disease patients and one of ordinary

skill in the art would have a reasonable expectation of success to use urine as a sample and use the method of Hoffman et al for the detection of early-stage renal disease. Further, the Hirawa et al reference discloses a relationship between the serum and urine concentrations that supports the Examiner position. Hirawa et al discloses that plasma L-PGDS concentration was slightly higher in the patients with diabetes mellitus than in the control subjects, whereas the urinary L-PGDS excretion almost doubles in the diabetic patients as compared with that in the control subjects (abstract).

Applicant further submitted three articles that describes the excretion patterns of heart fatty acid-binding protein (H-FABP) (Sohmiya et all J. Mol. Cardiol. 25: 1413-1426, 1993; Gorski et al. Clin. Chem. 43(1) : 193-195, 1997 ; and Hayashida et al. J. Cardiovasc. Sug. 42:735-740, 2001). These articles are not found persuasive because they are directed to a completely different protein that this structurally and functionally different than that of the instant claims and further, Applicant has not provided any evidence to suggest that the H-FABP would act or be expected to act the same in serum and urine as L-PGDS. Applicant argues that in view of the references that Hoffman et al in regard to L-PGDS by no means suggest, or would cause one of ordinary skill in the art to believe, that increased urinary L-PGDS levels are diagnostic of any kidney disease, let alone early kidney disease. This is not found persuasive because of reasons stated above and for reasons stated in the previous office action.

Allowable Subject Matter

8. Claims 37-40 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

9. The following is a statement of reasons for the indication of allowable subject matter: the prior art of record neither teaches nor suggests detecting the L-PGDS concentration and also determining a normal level of creatinine in the serum of the test subject or a step of determining the concentration of albumin in the urine of the test subject to be normal.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641

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01/04/05